Application instructions & Data Use Certification for NHLBI authorized access datasets

Revised 5 November, 2007

This document contains:

(1) the 4-step instructions for applying for Framingham SNP Health Association Resource (SHARe) data, and

(2) the Data Use Certification document that defines the terms of use for Framingham SHARe data.

Although requests to use Framingham SHARe data are submitted through the standard dbGaP request system http://view.ncbi.nlm.nih.gov/dbgap-controlled, requests for these data require additional information as described below.

Please read these instructions carefully and include all items in your application.

A complete application includes the following items.

- ☐ Information about your institution, including contact information for you and your Institutional Signing official[1]
- ☐ Details about your proposed research through an extended Research Use Statement[2]
- ☐ An abstract of the extended Research Use Statement (250 words)[1]
- ☐ A non-technical summary of your proposed research for public display (250 words)[1]
- ☐ Evidence of local IRB approval to conduct your research[2]
- ☐ Documentation of Human Subjects Training[2]
- ☐ A completed Data System Security Plan[2]
- ☐ A completed Staff Data Access Agreement Document[2]
- ☐ Biographical information about collaborators at your local institution. Collaborators at different institutions must submit separate applications for access to individual level data. Only include collaborators at your institution in this application.[1,2]

(1) denotes that the item is included in the SF424 R&R application generated by the dbGaP request system.

(2) denotes that the item must be included in a supplemental Adobe PDF document that will be uploaded during the application process and attached to the SF424 R&R.

Specific instructions for each of these items follow below.

Step 1

Prepare your extended research use statement & non-technical summary

Prepare a Research Use Statement for the requested dataset(s) of no more than 2,500 words, as well as an abstract of the Research Use Statement and a non-technical summary of the statement of no more than 250 words each.

- The RESEARCH USE STATEMENT will be reviewed by all NIH Institutes and Centers that are responsible for data included within your access request. The NHLBI will compare the RESEARCH USE STATEMENT to the *Limitations of Use* for the dataset(s) to confirm that it is consistent with the informed consents provided by participants in the original study.
- The non-technical summary for all approved research projects will be posted on the publicly available part of the dbGaP website.

> *Tip: Prepare and save the RESEARCH USE STATEMENT, associated abstract, and the non-technical summary in a word processing application. The abstract of the research use statement and the non-technical summary will be copied and pasted into their respective form boxes during the dbGaP request process. The statements will appear on page 3 of the final SF424 (R&R) application form. The full research use statement should be included as the first item in your supplemental PDF file described below.*

The RESEARCH USE STATEMENT must include:

(1) the hypotheses or questions to be addressed in the proposed data analysis,

(2) the phenotypes and covariates on which the analysis will focus,

(3) the clinical events that may be needed,

(4) any exclusions that are expected to be part of the analytic approach,

(5) the adequacy of the computing facilities to complete the proposed analyses, and

(6) a sufficiently detailed description of analytic methods for reviewers to determine whether the proposed key personnel have the qualifications to complete the proposed research.

Note: Applications that propose analyses focused primarily or exclusively on non-genetic objectives (phenotype-only analyses) will not be approved. Applicants interested in such analyses should consider whether NHLBI limited access data sets might meet their needs.

Information about those datasets is available at: www.nhlbi.nih.gov/resources/deca/default.htm.

Step 2

Collect Information about collaborators at your local institution

Compile a list of all collaborating investigators at your organization and a 2-page biosketch for each. You will need the list to correctly name your collaborators during the dbGaP access request process. The biosketches will be used in Step 3 as part of the supplemental information file.

Step 2 continued

- Your collaborators at different organizations must complete separate applications for the data signed by their appropriate local institutional official. NHLBI approvals are issued to organizations that are accountable for the actions of the individuals they sponsor.
- Coordinated requests by collaborating organizations should all use the same title in their applications and each should reference the others in their RESEARCH USE STATEMENT.

> *Tip: Required fields for listing collaborators in your application are First Name, Last Name, Street Address, City, Country, Zip, E-mail address, and Telephone number. Only collaborating investigators at your organization can be included.*

- By submitting an individual's name on a data access request, requesting organizations and their respective institutional signing officials affirm that the individuals cited as key personnel or staff have read and agreed to the terms and statements within the Data Use Certification (DUC) that follows these instructions.

Step 3

Prepare a supplemental information document in Adobe PDF format

Prepare a single Adobe PDF file that includes the following items in the order below. This file will be attached to your application during step 5 of the request process.

1. **Extended Research Use Statement**

   Start your supplemental information document with the full text of your extended research statement prepared in step 1.

2. **IRB Approval Document**

   The next item in sequence is you local Institutional Review Board (IRB) letter approving conduct of the proposed research project is required. Please note that only full or expedited approvals will be accepted.

3. **Documentation of Human Subjects Training**

   Follow with a letter addressed to the NHLBI DAC Chairperson listing all key personnel and staff associated with the research project who have completed human subjects training.

   All key personnel and all staff who will be manipulating individual level data or performing analyses must have human subjects training. The letter should state explicitly that the human subjects certification by all key personnel and other staff associated with the research project meets the minimum standard required by the NIH for clinical research grantees. The letter should be signed and dated by the PI named on the DUC. Proof of individual certification for human subject training is not requested.

4. **Data System Security Plan**

   Follow with a complete Data System Security Plan using the template available at

http://www.ncbi.nlm.nih.gov/projects/gap/pdf/SSP_Template.pdf. If an internal security plan is available, it may be provided in lieu of this template. The summary should not exceed 5 pages, but responses to all items in the template should be provided.

5. **Staff Data Access Agreement Document**

   Follow with scanned copies of the confidentiality awareness form available at http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/GetPdf.cgi?id=phd000316. Project staff signatures are required for all staff with access to Framingham SHARe data.

6. **Key Person Biosketches**

   Conclude with the set of 2-page biosketchs collected in step 2. A biosketch is required for each individual designated as key personnel on the SF424 (R&R) application form. Biosketches will be used to supplement the RESEARCH USE STATEMENT in determining whether the listed personnel have the qualifications to complete the proposed research.

Step 4

Complete the request for Framingham SHARe data in the NCBI dbGaP system

1) Log into the dbGaP request system at http://view.ncbi.nlm.nih.gov/dbgap-controlled using your eRA or NIH credentials. Instructions for obtaining an eRA account are available at https://commons.era.nih.gov/commons/registration/registrationInstructions.jsp.
2) Create a new research project and use the title as discussed in step 2 above.
3) Update your phone number in your personal preferences if necessary.
4) Select the appropriate institutional signing official.
5) Cut and paste the abstract of your research use statement into the box provided.
6) Cut and past the non-technical summary into the brief public summary box provided.
7) Enter the contact information for local collaborators from the list compiled in step 2.
8) Choose the appropriate Framingham SHARe data sets. There are 2 non-overlapping consent groups available. Note: only by requesting both the General research use and non-profit only data sets will the recipient receive the complete data set. Select (a) or (a and b) as appropriate:
   a. General research use – data for these participants may be requested by investigators at both non-profit and for-profit institutions
   b. Non profit only – data for these participants may be requested by investigators at non-profit institutions only.
9) Upload the supplemental PDF file prepared in step 3 above at “Edit Forms” step in the application wizard.
10) Click the check boxes to sign the form and route the request to your signing official for approval.

Framingham SNP Health Association Resource (SHARe) Project
Data Use Certification

The National Heart, Lung, and Blood Institute (NHLBI) and Recipient Organization (RECIPIENT) hereby enter into this Data Use Certification (DUC) as of the date specified on the NHLBI Data Access Committee (DAC) approval notification.

PRELIMINARY STATEMENT

The NHLBI has supported the collection of data from three generations in the Framingham Heart Study (FHS): the Framingham original cohort, the Framingham Offspring Study, and the Framingham Third Generation Study. The Framingham SHARe Project constitutes a unique scientific resource, consisting of extensive phenotypic information and genotypes for three generations of FHS participants. The NHLBI is committed to making the Framingham SHARe database available, on appropriate terms and conditions, to the largest possible number of qualified investigators in a timely manner.

Framingham SHARe data (genotype-phenotype datasets and pre-computed analyses of them) distributed by the National Center for Biotechnology Information of the National Institutes of Health through the dbGaP under this certification process include data elements that might enable identification of individual participants. Because of the extensive phenotype and genotype data included in the Framingham SHARe database, the NHLBI believes that the confidentiality and privacy of FHS participants can best be assured by requiring all who are interested in accessing the data to acknowledge their review of this DUC and agree to adhere to its provisions. Failure to comply with the provisions of this DUC would be considered in the review of all subsequent requests for access to Framingham SHARe Data and/or other NHLBI resources. Violation of its confidentiality provisions could lead to legal action on the part of FHS participants, their families, or the U.S. Government.

Note: RECIPIENT requests access to Framingham SHARe data for its PI at its sole risk.

DEFINITIONS

For purposes of this agreement

“DATA” is all information included in the Framingham SHARe database.

A Framingham Heart Study Investigator (FHS INVESTIGATOR) is an individual who

- is employed by the NHLBI to work on the FHS,
- has a current and active consulting agreement with the NHLBI, or
- has a current and active employment contract or consulting agreement with a contractor to the NHLBI to work on the FHS.

RECIPIENT is any organization that is seeking access to DATA, and may be a Public/State Controlled Institution of Higher Education; Private Institution of Higher Education; Nonprofit organization with 501(c)(3) IRS Status (Other than Institution of Higher Education); Nonprofit Organization without 501(c)(3) IRS Status (Other than Institution of Higher Education); Small Business; For-Profit Organization (Other than Small Business); State Government; Government of a U.S. Territory or Possession; Non-domestic (non-U.S.) Entity (Foreign Organization); or Eligible Agency of the U.S. Government.

Principal Investigator (PI) is an individual employed by RECIPIENT who will lead the scientific investigation proposed in the application, oversee the supporting staff who are provided access to the data and contribute to the analytic effort and public disclosure of study results, and assume responsibility for all team members’ compliance with the terms and conditions of this DUC.

APPROVED USERS are PIs and all other individuals specifically identified as key personnel or staff with access to DATA on a DUC that has been approved by the NHLBI DAC.

Authorized Institutional Business Official is an individual with the authority to enter into business transactions on behalf of RECIPIENT.

AGREED TERMS AND CONDITIONS

1. Research Project.

    1.1. DATA will be used by PI solely in connection with the biomedical genetic research project (RESEARCH PROJECT), specifically described in an attachment designated "SF424 (R&R)." **Note**: Applications to use DATA to conduct non-genetic research or to investigate individual pedigree structures, individual participant genotypes, or issues such as non-paternity will not be approved.

    1.2. This DUC covers only the RESEARCH PROJECT specifically described in the associated SF424 (R&R). RECIPIENT will submit a completed SF424 (R&R) for each research project for which DATA are requested.

2. Non-transferability. This DUC is not transferable. RECIPIENT agrees that prior to the implementation of any changes to the RESEARCH PROJECT, and/or of the appointment by RECIPIENT of another PI to complete the RESEARCH PROJECT, RECIPIENT will execute and submit a new DUC in which the new PI and/or changes to RESEARCH PROJECT are described.

3. Publication. Prompt publication or public disclosure of the results of research using Framingham SHARe data is encouraged. However, the Framingham SHARe is the product of substantial efforts by FHS INVESTIGATORs and other contributing investigators. Therefore, RECIPIENT agrees to adhere to the following policy: All FHS INVESTIGATORs, non-FHS investigators who have provided ancillary genotype and phenotype study data, and designees assigned by the SHARe Oversight Committee who have applied for and received access to the data may publish results at any time. Investigators who are neither FHS INVESTIGATORs, non-FHS investigators who have provided ancillary study data, nor designees assigned by the SHARe Oversight Committee to conduct analyses and who are Approved Users with access to the SHARe database will agree not to submit (or show to editors for pre-review) publications, including abstracts and manuscripts, until twelve (12) months have elapsed from the later of the date of release of the Framingham SHARe Database or the date of the most recent update thereof. RECIPIENT agrees to provide to the NHLBI a copy of any abstract five (5) business days in advance of submission for publication and any manuscript two (2) weeks in advance of submission for publication, in order to permit administrative review and comment and to assess compliance with the confidentiality and other requirements of this Agreement.

4. Non-Identification. RECIPIENT agrees not to use DATA, either alone or in conjunction with any other information**,** in any effort to establish the identities of or make contact with any FHS participants.

5. Use Limited to Research Project. RECIPIENT agrees that DATA will not be used in any research that is not disclosed and approved as part of the RESEARCH PROJECT. RECIPIENT also agrees not to use DATA for purposes unrelated to biomedical genetic research.

6. No Distribution. RECIPIENT agrees to retain control over DATA, and further agrees not to transfer DATA, with or without charge, to any other entity or any individual other than

APPROVED USERS or other research staff of RECIPIENT's PI, who also agree to the provisions of the DUC, subject to applicable law.

7. Intellectual Property. By requesting access to DATA, RECIPIENT and RECIPIENT's PI acknowledge the intent of the NHLBI to see that all recipients follow the Framingham SHARe Intellectual Property (IP) Policy, as summarized below:

   7.1. Achieving maximum public benefit is the ultimate goal of the NHLBI. The NHLBI believes that the contents of the Framingham SHARe should be considered as pre-competitive, and urges users to avoid making IP claims on DATA. However, the NHLBI also recognizes the importance of the later development of IP on downstream discoveries, especially in therapeutics, which will be necessary to support full investment in products to benefit the public

   7.2. In this spirit, it is expected that the contents of the Framingham SHARe and conclusions derived therefrom will remain freely available, without requirement for licensing, for applications such as, but not necessarily limited to, the following: the use of markers in developing assays and diagnostic tools employing a variety of single or multiple technical platforms; the use of combinations of markers in multiplex assays; and, the use of markers as guides toward identification of new drug targets.

   7.3. The NHLBI encourages consistency with the recommendations cited in the NIH Best Practices for the Licensing of Genomic Inventions and in the NIH Research Tools Policy http://www.ott.nih.gov/policy/lic_gen.html .

8. Non-Data. Notwithstanding the definition of DATA or the provisions of this DUC, RECIPIENT's obligations under this DUC shall not extend to any information that:

   8.1. can be demonstrated to have been publicly known at the time of disclosure; or

   8.2. can be demonstrated to have been in the possession of or that can be demonstrated to have been readily available to RECIPIENT from another source prior to the disclosure; or

   8.3. becomes part of the public domain or publicly known by publication or otherwise, not due to any unauthorized act by RECIPIENT; or

   8.4. can be demonstrated as independently developed or acquired by RECIPIENT without reference to or reliance upon DATA provided under this data access request; or

   8.5. is required to be disclosed by law, provided the RECIPIENT takes responsible and lawful actions to avoid and/or minimize such disclosure.

9. Non-Endorsement, Indemnification. RECIPIENT agrees not to claim, infer, or imply endorsement by the U.S. Government of the RESEARCH PROJECT, the entity, or personnel conducting the RESEARCH PROJECT. To the extent permitted by law, RECIPIENT agrees to hold the U.S. Government, FHS Investigators, and all other investigator(s) who generated DATA and the agents and employees of each of them harmless and to defend and indemnify all such parties for all liabilities, demands, damages, expenses, and losses arising out of RECIPIENT's use, for any purpose, of DATA.

10. RECIPIENT's Compliance with IRB Requirements. RECIPIENT acknowledges that the conditions for use of these DATA are not exempt from review and, if RECIPIENT is subject to U.S. law, have been approved by the RECIPIENT's Institutional Review Board (IRB)

operating under an Office of Human Research Protections (OHRP)-approved Assurance and in accordance with Department of Health and Human Services regulations at 45 CFR Part 46 or, if RECIPIENT is not subject to U.S. law, have been approved by the responsible authority for the country in which RECIPIENT is located. RECIPIENT agrees to comply fully with all such conditions. RECIPIENT agrees to report promptly to the NHLBI any proposed change in the RESEARCH PROJECT and any unanticipated problems involving risks to subjects or others. This DUC is made in addition to, and does not supersede, any of RECIPIENT's institutional policies or any local, State, and/or Federal laws or regulations that provide additional protections for human subjects.

11. Termination. The NHLBI may terminate data access under this DUC if RECIPIENT is in default of any provisions of this DUC and such default has not been remedied within 30 days after the date of written notice by NHLBI's Authorized Representative of such default.

12. Failure to Comply. Failure to comply with any of the provisions of this DUC would be considered in the review of all subsequent requests for further access to Framingham SHARe and/or other NHLBI resources. In addition, the U.S. Government shall have the right to institute and prosecute any available proceeding at law or in equity against RECIPIENT for violating or threatening to violate the confidentiality requirements of this DUC, the limitations on the use of DATA, or both. Proceedings may be initiated against the violating party, legal representatives, and assigns, for a restraining injunction, compensatory and punitive damages, mandamus, and/or any other proceeding in law or equity, including obtaining the proceeds from any intellectual property or other rights that are derived in whole or in part from the breach of the confidentiality requirements or use limitations of this agreement. In addition, RECIPIENT acknowledges and agrees that a breach or threatened breach of the confidentiality requirements or use limitations of this DUC may subject RECIPIENT to legal action on the part of FHS participants, their families, or both.

13. Accurate Representations. RECIPIENT expressly certifies that the contents of any statements made or reflected in this document are truthful and accurate.

14. Duplication of Research. RECIPIENT acknowledges that other researchers have access to Framingham SHARe data so that duplication of research is possible.

15. Annual Reporting. By requesting access to the Framingham SHARe database, RECIPIENT and RECIPIENT's PI acknowledge the intent of the NHLBI to see that all recipients provide the NHLBI with a report every twelve (12) months during the term of this DUC containing 1) a summary of genetic analyses conducted by RECIPIENT; 2) a listing of all accepted abstracts and publications; and 3) evidence of continuing IRB approval in the performance of the Research Project. Such report should cover all genetic analysis derived by RECIPIENT up to six (6) months before the reporting date. Annual reports for Years 1 and 2 of this DUC should be submitted the first day of the month following the anniversary date of this DUC (as indicated by the date the data were made accessible to the APPROVED USER). The Year 3 annual report should be submitted by the last day of the month following the anniversary of the effective date of this DUC.

    In addition to annual reporting, RECIPIENT and RECIPIENT's PI agree to notify the NHLBI DAC of any breaches in data security or adverse events within three (3) business days of when the RECIPIENT or RECIPIENT's PI were notified of the event. The notification should include the date and nature of the event, what was done to address it, and what is being done to prevent further problems.

    All reports and notifications should be sent to:
    NHLBI Data Access Committee Chair
    Email: nhlbigeneticdata@mail.nih.gov
    FAX: 301-480-1455

16. Acknowledgement. Because of the substantial long-term contribution of FHS INVESTIGATORS in obtaining the phenotypic data in Framingham SHARe, the NHLBI believes that their contribution should be appropriately acknowledged by all APPROVED USERs of DATA.

    Therefore, RECIPIENT and RECIPIENT's PI agree to ensure that the contribution of the NHLBI and FHS INVESTIGATORS are acknowledged in any and all oral and written presentations, disclosures, and publications resulting from any and all analyses of DATA. In addition, for genetic analysis using ancillary study data, RECIPIENT and RECIPIENT's PI agree to ensure that the contribution of the ancillary study principal investigators are acknowledged in any and all resulting oral and written presentations, disclosures, and publications.

    If the RESEARCH PROJECT involves a collaboration with FHS INVESTIGATORS, then RECIPIENT and RECIPIENT's PI will ensure that FHS INVESTIGATORS are acknowledged as co-authors, as appropriate, on any publication.

    If the RESEARCH PROJECT does not involve collaboration with FHS INVESTIGATORS, then the manuscript shall include the acknowledgement below.

    > "The Framingham Heart Study is conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with Boston University. This manuscript was not prepared in collaboration with investigators of the Framingham Heart Study and does not necessarily reflect the opinions or views of the Framingham Heart Study, Boston University, or the NHLBI."

Addendum to the Data Use Certification Agreement
Modification of Data Security Terms and Best Practices

Effective for all dbGaP Data Access Requests submitted on or after March 23, 2015,
Section 6 of the Data Use Certification Agreement is replaced in its entirety by the following:

6. Data Security and Data Release Reporting

The Requester and Approved Users, including the institutional IT Director, acknowledge NIH's expectation that they have reviewed and agree to manage the requested dataset(s) according to the current NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy and the institutional IT security requirements and policies, and that the institution's IT security requirements and policies are sufficient to protect the confidentiality and integrity of the NIH controlled-access data entrusted to the Requester.

If approved by NIH to use cloud computing for the proposed research project, as outlined in the Research and Cloud Computing Use Statements of the Data Access Request, the Requester acknowledges that the IT Director has reviewed and understands the cloud computing guidelines in the NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy.

Requesters and PIs agree to notify the NHLBI DAC of any unauthorized data sharing, breaches of data security, or inadvertent data releases that may compromise data confidentiality within 24 hours of when the incident is identified. As permitted by law, notifications should include any known information regarding the incident and a general description of the activities or process in place to define and remediate the situation fully. Within 3 business days of the NHLBI DAC notification, the Requester, through the PI and the Institutional Signing Official, agree to submit to the NHLBI Data Access Committee a detailed written report including the date and nature of the event, actions taken or to be taken to remediate the issue(s), and plans or processes developed to prevent further problems, including specific information on timelines anticipated for action.

All notifications and written reports of data security incidents should be sent to:
NHLBI Data Access Committee URGENT: nhlbigeneticdata@nhlbi.nih.gov
GDS mailbox: gds@mail.nih.gov

NIH, or another entity designated by NIH may, as permitted by law, also investigate any data security incident. Approved Users and their associates agree to support such investigations and provide information, within the limits of applicable local, state, and federal laws and regulations. In addition, Requesters and Approved Users agree to work with the NHLBI and NIH to assure that plans and procedures that are developed to address identified problems are mutually acceptable and consistent with applicable law.

Addendum to the Data Use Certification

Effective for all dbGaP study datasets registered prior to July 31, 2013

- Annual Data Use Reports will no longer be submitted by email to the relevant Data Access Committee(s) (DACs), as stated in the Data Use Certification(s) associated with the datasets you are requesting.

- Principal Investigators are now expected to submit online research progress updates through the dbGaP system, as part of the annual renewal process or close-out process.